

## REMARKS

Claims 1, 3, 4, 6, 8-17, 19-21, 23, and 24 are pending in the application and stand rejected. Claims 1 and 21 have been amended. Claim 16 has been canceled. No new matter has been introduced. Reconsideration and allowance of Claims 1, 34, 6, 8-15, 17, 19-21, 23, and 24 is respectfully requested.

### The Rejection of Claims 1, 3-4, 6, 8, 10, 12-21, and 23 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent Publication No. 2011/0076675 (Jacobsen et al.)

Claims 1, 3-4, 6, 8, 10, 12-21, and 23 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent Publication No. 2011/0076675 (Jacobsen et al.). Applicants respectfully traverse this ground of rejection for at least the following reasons.

While not acquiescing to the Examiner's position, but in order to facilitate prosecution, Claim 1 has been amended to incorporate the limitation of dependent Claim 16, now canceled.

Claim 1, as amended, recites:

A method for amplifying a microRNA molecule to produce DNA molecules, the method comprising the steps of:

- (a) producing a first DNA molecule that is complementary to a target microRNA molecule using primer extension with an extension primer comprising a first portion having a length from 3 to 17 nucleotides selected to hybridize to a portion of the target microRNA molecule and a second portion that hybridizes to the complement of a universal forward primer; and
- (b) amplifying the first DNA molecule to produce amplified DNA molecules using the universal forward primer and a reverse primer,

wherein the reverse primer is selected to specifically hybridize to a portion of the first DNA molecule that is complementary to the target microRNA molecule under defined hybridization conditions, and wherein ~~at least one of the universal forward primer and~~ the reverse primer comprises at least one locked nucleic acid molecule.

Independent Claim 21 has been similarly amended at step (2), which now recites:

(2) amplifying the first DNA molecule to produce amplified DNA molecules using the universal forward and a reverse primer, wherein the reverse primer is selected to specifically hybridize to a portion of the first DNA molecule that is complementary to the target microRNA molecule under defined hybridization conditions, and wherein ~~at least one of the universal forward primer and~~ the reverse primer comprises at least one locked nucleic acid molecule . . . .

Support for this amendment is found in original Claim 16, now canceled, and in the specification as filed; for example, at page 2, lines 31–33; page 3, lines 11–13; page 5, lines 15–19; page 9, line 28, to page 10, line 11; and Figure 1. With regard to dependent Claim 16, which limitation is now incorporated into Claims 1 and 21, the Examiner acknowledges that while Jacobsen discloses the use of an LNA modified extension primer, Jacobsen does not specifically teach that the reverse primers in the embodiment depicted in Figure 11 comprise LNA modifications. Further in this regard, it is noted that as described in the instant specification, through experimentation, applicants have determined, "[A]lthough one or more LNAs can be included in any of the primers used in the practice of the present invention, it has been found that the efficiency of synthesis of cDNA is low if an LNA is incorporated into the extension primer. While not wishing to be bound by theory, LNAs may inhibit the activity of

reverse transcriptase." Page 10, lines 8-11. Therefore, the portions of Jacobsen relied upon by the Examiner, which describe the use of LNA modified extension primers, teach away from the claimed invention, as amended, which recites the use of an LNA modified reverse primer.

Therefore, it is demonstrated that a *prima facie* case of obviousness has not been established because the cited reference fails to teach or suggest all the limitations of the claimed invention, as amended. Accordingly, removal of this ground of rejection is respectfully requested.

The Rejection of Claims 9, 11, and 24 Under 35 U.S.C. § 103(a) as Being Unpatentable Over Jacobsen in View of Crollius in View of Buck and Further in View of Spivack

Claims 9, 11, and 24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Jacobsen et al. in view of Crollius et al. in view of Buck et al. and further in view of Spivack et al. Applicants respectfully traverse this ground of rejection for at least the following reasons.

Claims 9 and 11 depend from Claim 1. Claim 24 depends from Claim 21. As noted above, Claims 1 and 21 have been amended to incorporate the limitation of Claim 16, which has been canceled. Claims 9, 11, and 24 are believed to be patentable over Jacobsen et al. for at least the reasons described above in connection with the rejection of Claims 1 and 21. For example, Jacobsen does not teach the use of a reverse primer comprising at least one locked nucleic acid molecule.

The teachings of Crollius, Buck, and Spivack et al. fail to cure the deficiencies of Jacobsen in this regard.

The Examiner cites Crollius as disclosing an extension primer comprising the nucleic acid sequence of SEQ ID NO:1 and wherein the universal forward primer consists of the nucleic acid sequence set forth in SEQ ID NO:13. The Examiner characterizes Buck as demonstrating the equivalence of primers selected by various different criteria for amplifying a target sequence.

It is noted that there is no teaching or remote suggestion in Crollius or Buck with regard to a method using a reverse primer comprising at least one locked nucleic acid molecule, as claimed.

The Examiner cites Spivack as teaching a method of measuring the amount of amplified DNA using fluorescence-based quantitative PCR. Spivack does not teach or suggest the use of the reverse primer sequences comprising at least one LNA as recited in Claims 1 and 21 as amended.

Therefore, it is demonstrated that a *prima facie* case of obviousness has not been established because Jacobsen et al., Crollius et al., Buck et al., and Spivack, taken together or separately, fail to teach or suggest every limitation of Claim 1, from which Claims 9 and 11 depend, and Claim 21, from which Claim 24 depends. Thus, as with Claims 1 and 21, as amended, these dependent claims are also not obvious over the cited art. Accordingly, removal of this ground of rejection is respectfully requested.

#### Conclusion

In view of the foregoing amendments and remarks, it is submitted that all the pending claims are in condition for allowance. Reconsideration and favorable action are requested. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicant's attorney at 206.695.1655.

Respectfully submitted,

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